The inverse association between parity and bone health is independent of lifestyle in postmenopausal Chinese women

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Abstract. This study aimed to investigate the association between parity and bone mineral density in postmenopausal Chinese women, as well as the interference of physical activity and sedentary time on this association. A total of 1,712 participants were enrolled in this study. Participants were separated into three groups according to the number of parities: group 1, 1–2; group 2, 3–4; group 3, ≥5. Physical activity level was assessed according to the International Physical Activity Questionnaire. Calcaneus bone mineral density (BMD) and bone quality were assessed by qualitative ultrasound. As a result, logistic regression showed that compared to that in group 1, the risk of fracture in group 3 was increased significantly (p < 0.001). A greater number of parities was associated with a lower BMD, broadband ultrasonic attenuation (BUA), quantitative ultrasound index (QUI), speed of sound (SOS), and T-score among the three groups after adjustment for age (All p for trend < 0.05). The number of parities was an independent factor negatively correlated with BMD, BUA, QUI, SOS, and T-score (All p < 0.05). BMD, BUA, QUI, SOS, and T-score were significantly increased in the physically active participants independent of parity (all p < 0.05), and decreased in the sedentary participants independent of parity (p < 0.05, except BUA). A great number of parities was negatively associated with bone health. Physical activity was positively correlated and sedentary time was negatively correlated with bone health independent of parity.

Key words: Physical activity, Sedentary, Parity, Bone health

OSTEOPOROSIS has become a significant health problem because of the high disability, mortality, and health-care costs resulting from osteoporosis fracture [1]. However, it is continuously underdiagnosed and undertreated. Therefore, it is very important to screen risk of osteoporosis for prevention. Osteoporosis is affected by numerous factors, such as ethnic origin, menstrual status, socioeconomic status, physical activity, sedentary time, parity, lactation, and so on [2-5]. The results of prospective and retrospective studies about effect of parity on bone mineral density (BMD) in postmenopausal women are inconsistent. However, for populations with high parity from developing countries, such as India [6], Turkey [7], and Morocco [8], multiparity was detrimental to BMD. To our knowledge, no study has been performed in Chinese women, an ideal population in which there are many pregnancies, to explore the influence of parity on BMD.

Previous studies have demonstrated that physical activity is not only associated with improved BMD and bone microarchitecture in children and young adults [9], but also protects bone health in older women and men [10]. Nevertheless, existing data on associations between bone health and physical activity in parous women was sparse. Meanwhile, in view of emerging evidence showing the positive effects of physical activity on bone metabolism, other studies have demonstrated the unique impact of sedentary time on bone health independent of physical activity [11]. Therefore, additional study is necessary to illustrate the interference of lifestyle on the association between parity and bone health, especially for women in modern society, who are accustomed to reduced physical activity and increased sedentary time, and are therefore prone to osteoporosis.

The goal of the present study was to investigate the association between parity and bone health in postmenopausal women, as well as the interference of physical activity and a sedentary lifestyle on this association.
Subjects and Methods

Study design

This cross-sectional study was a part of a REACTION study [12], which was conducted between June 2011 and January 2012 among 259,657 adults aged more than 40 years in 25 communities across China. Postmenopausal women were included in the present study. We defined parity as the self-reported number of live births.

Exclusion criteria were as follows:

1) taking drugs known to influence bone metabolism, such as vitamin D, calcium, glucocorticoids, heparin, immunosuppressors, estrogen, progesterone, bisphosphonates, antiepileptic drugs, and antithyroid drugs; 2) chronic liver disease, chronic renal disease; thyroid disease, parathyroid disease, hypopituitarism, acromegaly or adrenal disease, 3) malignancy; 4) hysterectomy; 5) connective tissue disease.

Finally, a total of 1,712 postmenopausal women were enrolled in this study. This study was conducted in accordance with the Declaration of Helsinki and approved by the Ruijin Hospital Ethics Committee, Shanghai JiaoTong University School of Medicine (201114RHEC). All participants provided written informed consent prior to participation in the study.

Questionnaire

Each participant was required to complete a standard validated questionnaire administered by trained interviewers. The self-report questionnaire involved questions assessing demographics, lifestyle factors (physical activity, and total sitting time per week), menopausal status, reproductive history, and medical history.

Physical activity level was evaluated according to the International Physical Activity Questionnaire [13], which contains with questions on the frequency and duration of moderate and vigorous activities. Physically active was defined as moderate-to-vigorous-intensity physical activity (MVPA) ≥30 minutes per week, and physically inactive was defined as MVPA <30 minutes per week. A cutoff of 1,740 minutes per week spent on sitting was used to define a sedentary lifestyle.

Anthropometric and biochemical measurements

Each participant was required to undergo a general physical examination by trained doctors. Body height, weight, waist circumference (W), and blood pressure (BP) were recorded by standard methods. Body mass index (BMI) was calculated as body weight (kilograms) divided by height (meters) squared. A 75-g oral glucose tolerance test was administered after an overnight fast, and blood samples were drawn at 0 and 120 minutes for plasma glucose measurements. Fasting plasma glucose (FPG), 2-hour plasma glucose (2hPG), glycated hemoglobin (HbA1c), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), triglycerides (TG), and total cholesterol (TC) were measured using chemiluminescence methods with an autoanalyzer. All serum lipids were measured in the fasting state. The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as follows: HOMA-IR = FINS (mU·l⁻¹) × FPG (mmol·l⁻¹)/22.5.

Ultrasound measurement

BMD and quality were assessed by qualitative ultrasound (QUS) measurements of the dominant calcaneus using an Achilles Express Ultrasound (GE Lunar Corp) in Wuyishan and a Sahara (Hologic) in Ningde. Speed of sound (SOS (m/s)) refers to the division of transmission time of sound waves by the length of the body part studied, and broadband ultrasonic attenuation [BUA] (dB/MHz) refers to the slope between the attenuation of sound signals and their frequency [14]. The quantitative ultrasound index [QUI] is a composite parameter derived from the BUA and SOS. An estimate of heel BMD (Est.heel BMD) with units of grams per square centimeter using the following equation: Estimated heel BMD = 0.002592 × (BUA + SOS) – 3.687 (g/cm²). The SI-derived T-score was the only parameter we used to assess BMD. T-score for BMD were calculated using a database of young, healthy Chinese individuals from the same study area as the reference. The ultrasound parameters were measured twice on the dominant calcaneus by a doctor trained in the use of the QUS systems, and the mean value was used for analysis. Both QUS instruments were calibrated daily according to the manufacturer’s recommendations before measurements were taken. QUS has several advantages including low cost, portability and no exposure to ionizing radiation. T-score threshold of −1.8 was deemed to be appropriate for diagnosing osteoporosis using QUS [14], and was used to diagnose osteoporosis in the present study.

Statistics analyses

Statistical analyses were performed with SPSS version 16.0 (SPSS Inc., Chicago, IL, 167 USA). For continuous variables, data are presented as the mean ± standard deviation or median with interquartile range, and for categorical variables, data are presented as numbers (percentages). Comparisons between two groups were carried out by an unpaired Student’s t-test, Mann-Whitney U-test and Chi-squared test for continuous and categorical variables, respectively. Binary logistic regression are used to estimate the association of fractures and parity. Multiple stepwise regression analysis was performed to identify independent factors affecting BMD. Analyses of
variance were applied to explore the interaction of physical activity or sedentary and parity on BMD. The threshold of statistical significance was set at 0.05 for two-tailed p-values.

Results

Clinical characteristics of the study participants

A total of 1,712 postmenopausal women were enrolled in the present study, and divided into three groups according to parity: group 1, 1–2 children, group 2, 3–4 children, and group 3, ≥5 children. Among groups of different parities, the trends of age, BMI, WC, HbA1c, and systolic blood pressure (SBP) increased (all p < 0.05). And the trends of HDL-c, BMD, BUA, QUI, SOS, T-score declined (all p < 0.05, Table 1).

Association between parity and fractures

The prevalence of fracture in groups 1–3 was 7.77%, 7.79%, 18.46% respectively. Defining the presence of fracture as the dependent variable and group 1 as the reference, logistic regression showed that the odds ratio (OR) increased significantly in the group 3 (OR = 2.670, 95% confidence intervals [CI]: 1.711–4.166, p < 0.001, Fig. 1).

Multivariate linear stepwise regression analysis of parity and indexes of osteoporosis

The results of the covariance analysis showed a decreasing trend in all of the indexes of bone health (BMD [p for trend < 0.001], BUA [p for trend < 0.001], QUS [p for trend < 0.001], SOS [p for trend = 0.040], and T-score [p for trend = 0.010]) among the three groups after adjustment for age.

A further multivariate linear regression analysis was conducted. Fertility condition, age, BMI, HOMA-IR, HbA1c, TG, HDL-c, LDL-c, SBP, and DBP were defined as independent variables, and BMD, BUA, QUI, SOS, and T-score were taken as dependent variables respectively. The results showed that fertility condition was an independent and negative factor of BMD (standardized β = –0.108, p < 0.001), BUA (standardized β = –0.115, p < 0.001), QUI (standardized β = –0.107, p < 0.001), SOS (standardized β = –0.075, p < 0.001) and T-score (standardized β = –0.110, p < 0.001) (Table 2).

Table 1: Clinical characteristics

<table>
<thead>
<tr>
<th></th>
<th>Group 1 Parity 1–2</th>
<th>Group 2 Parity 3–4</th>
<th>Group 3 Parity ≥5</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>798</td>
<td>719</td>
<td>195</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (years)</td>
<td>55.00 (52.0–59.0)</td>
<td>61.0 (55.0–67.0)</td>
<td>67.0 (62.0–74.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>23.84 (21.64–25.65)</td>
<td>24.36 (22.22–26.56)</td>
<td>24.89 (22.37–26.84)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Parity</td>
<td>2 (1–2)</td>
<td>3 (3–4)</td>
<td>5 (5–6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>W (cm)</td>
<td>79.18 ± 8.31</td>
<td>81.86 ± 8.63</td>
<td>83.65 ± 10.01</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.90 (5.60–6.20)</td>
<td>6.00 (5.70–6.40)</td>
<td>6.10 (5.80–6.53)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>HDL-c (mmol/L)</td>
<td>1.32 (1.11–1.56)</td>
<td>1.24 (1.06–1.46)</td>
<td>1.15 (0.93–1.40)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LDL-c (mmol/L)</td>
<td>3.13 (2.54–3.76)</td>
<td>3.05 (2.46–3.62)</td>
<td>2.85 (2.19–3.54)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>TG (mmol/L)</td>
<td>1.25 (0.91–1.79)</td>
<td>1.32 (0.98–1.87)</td>
<td>1.29 (0.91–1.83)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>129.00 (116.00–142.10)</td>
<td>135.00 (121.67–151.67)</td>
<td>142.00 (127.67–159.00)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>74.67 (67.67–82.00)</td>
<td>74.00 (68.00–82.00)</td>
<td>74.00 (67.33–82.67)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>BMD (g/cm²)</td>
<td>0.50 (0.42–0.60)</td>
<td>0.46 (0.39–0.55)</td>
<td>0.41 (0.34–0.49)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BUA (dB/MHz)</td>
<td>72.34 (59.98–85.01)</td>
<td>65.98 (55.51–77.70)</td>
<td>57.61 (48.97–69.00)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>QUI</td>
<td>91.55 (79.80–106.50)</td>
<td>84.71 (73.09–99.32)</td>
<td>76.46 (65.96–89.26)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SOS (m/s)</td>
<td>1,543.18 (1,524.30–1,569.10)</td>
<td>1,532.80 (1,514.90–1,557.20)</td>
<td>1,522.00 (1,504.00–1,539.50)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>T-score</td>
<td>–0.70 (–1.50–0.30)</td>
<td>–1.10 (–1.90–0.20)</td>
<td>–1.60 (–2.30–0.80)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Note: BMI, body mass index; W, waist circumference; HbA1c, glycated hemoglobin A1c; HOMA-IR, homeostasis model assessment-insulin resistance; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; TG, triglyceride; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMD, bone mineral density; BUA, broadband ultrasonic attenuation; QUI, lower quantitative ultrasound index; SOS, speed of sound.

Data are median (interquartile range).

P for trend from group 1 to group 3.
Interference of physical activity and sedentary time on the association between parity and bone mineral density

Covariance analysis showed that BMD ($p = 0.001$), BUA ($p = 0.003$), QUI ($p = 0.001$), SOS ($p = 0.019$), and T-score ($p = 0.001$) in physical active group were significantly higher than those in physical inactive group regardless of parities. The inverse association between parity with BMD, BUA, QUI, SOS and T-score was not interfered by the effect of physical active on BMD, BUA, QUI, SOS and T-score (all $p < 0.05$, Fig. 2). BMD ($p = 0.006$), QUI ($p = 0.006$), SOS ($p = 0.005$), and T-score ($p = 0.007$) in sedentary lifestyle group were significantly lower than those in nonsedentary lifestyles group regardless of parities. The inverse relationship between parity with BMD, BUA, QUI, SOS and T-score was not interfered by the effect of sedentary lifestyle on BMD, BUA, QUI, SOS and T-score (all $p < 0.05$, Fig. 3).

Discussion

The present study revealed that parity was inversely correlated with bone health. As the number of parities increased, the risk of fracture increased in postmenopausal women. Regardless of the number of parities, physical activity was positively associated and a sedentary lifestyle was negatively associated with bone health. The association of BMD with parity and its association with sedentary time were also independent of each other. Glucose and lipid metabolism might be correlated with bone metabolism [15, 16], and the present study showed that there were differences in HbA1c and HDL-c among groups of different parities, so in addition to fertility condition, age, BMI, W, SBP, and DBP, HbA1c, HOMA-IR, HDL-c, LDL-c, and TG were also analyzed in the multiple linear regression analyses. The results showed that fertility was an independent factor positively associated...
with BMD.

To provide a sufficient calcium supply to the fetus for skeletal growth during pregnancy and to the newborn infant in the form of adequate maternal milk production during lactation, the physiological demand for calcium is approximately 30 g of calcium for a full-term singleton [17]. To meet the fetal demand during the third trimester, intestinal calcium absorption increases, renal calcium excretion decreases, and skeletal resorption of calcium increases, but the adaptation is inadequate. Thus, bone mass could decrease in association with parity [18]. In a hospital-based cross sectional study from India, parity was negatively correlated with the BMD of neck of the femur, trochanter, lumbar spine, and forearm [6]. In a study from Turkey, low BMD was associated with high parity in postmenopausal women [7]. Similar research demonstrated that low BMD of the spine and hip in postmenopausal women with parity greater than six [8]. We et al. discovered that the prevalence of osteoporosis was higher in women with a higher number of parities than in

Fig. 2 Interference of physical activity with the association of BMD (a), BUA (b), QUI (c), SOS (d), and T-score (e) with parities.

Fig. 3 Interference of physical sedentary with the association of BMD (a), BUA (b), QUI (c), SOS (d), and T-score (e) with parities.
women with a lower number of parities [19]. However, some studies have shown no correlation or a positive correlation between BMD and parity [20-22]. A meta-analysis demonstrated that parity has a positive effect on bone in healthy women. However, most populations included in this review were Caucasian except for one population that was from Asia, and many studies did not provide BMD values adjusted for age and BMI [23]. Therefore, the discrepancies between the above studies might be explained by different number of parities, ethnicities, socioeconomic statuses, and distinct nutrition. In line with most previous studies from developing countries, the present study suggested that a higher number of parities was associated with decreased BMD in adult women, and that parity was an independent factor correlated with bone health.

Although no unique relevant studies have reported an association among physical activity, parity, and BMD in women, a previous study showed that exercise had elevated lumbar spine BMD as compared with women who did not exercise during the first year postpartum [24]. Another study demonstrated that the decrease in BMD in women during pregnancy engaged in active exercise was less than that in women who were inactive [25]. Exercise not only improved BMD in children and youth, but also increased BMD and improved bone architecture in postmenopausal women and elderly men. Furthermore, physical activity could prevent falls and fall-related injuries in the elderly individuals [26]. In addition, some studies demonstrated that mechanical stimulation caused by physical activity might result in increased bone mineralization, periosteal diameter, and cortical thickness [27]. The present study also showed that even with high parity, BMD in the moderate-to-vigorous-intensity physically activity group was higher than that in the inactive group. Our study suggested that although higher parity was associated with poor bone health regardless of physical activity, physical activity could contribute to increased BMD in adult women irrespective of the number of deliveries.

Wang et al. found that sedentary time in prepuberty was negatively correlated with young adult bone mass [28]. A study from the National Health and Nutrition Examination Survey (NHANES) suggested that sedentary behavior contributed to decreases in BMD and BMC at the femoral neck, regardless of physical activity status [29]. BMD in the sedentary participants in our study was lower than that in the non-sedentary participants. Both sedentariness and parity could influence BMD in women independently of each other. Hence, improving lifestyle, which includes increasing physical activity and reducing sedentary time, is important to women’s bone health.

The potential mechanisms underlying the inverse relationship between parity and BMD remain to be determined. Studies in mice and rats have indicated that a decrease in trabecular bone density is irreversible as the number of litters increases [30, 31]. Furthermore, the deterioration of cortical and trabecular bone microarchitecture and matrix mineralization density persists even 3 years after the resumption of regular menses in women [32]. Thus, bone loss may be incompletely restored when the number of parities increases. Nevertheless, the association between parity and bone health is inconsistent, and the mechanisms behind the effect of parity on the skeleton are complex. Therefore, further basic and clinical studies are necessary to address the etiology of the effect of parity on the skeleton, and to define the relationship.

The present study remained some limitations. First of all, this was a cross-section study, so we cannot obtain a cause-and-effect relationship. For another, the present study population was restricted to the residents of the southeast city. Therefore, our findings should be verified and generalized in a larger population in the future studies. In addition, the policy would be taken into account in the future studies. Future studies are needed to base upon more large survey sample to contain the population of null-parous women. Detection of estrin level would be needed in the future studies.

In conclusion, the number of parities was an independent and negative factor of bone health. Regardless of the number of parities, increasing physical activity and reducing sedentary time are important for bone health in postmenopausal Chinese women.

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Disclosure Statement

The authors declare that they have no conflicts of interest.
Parity and bone mineral density

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